There are many causes of hypercalcemia but the following three are the most common: primary hyperparathyroidism, neoplasm and sarcoidosis. In primary hyperparathyroidism, hypercalcemia is associated with circulating parathyroid hormone levels in the high or high-normal range and elevated urinary secretion of adenosine 3′:5′-cyclic phosphate. A subnormal serum albumin concentration is a key feature of the hypercalcemia due to neoplasm; 1,25-(OH)2-D_3 levels are usually elevated. The serum chloride level is low in some patients with hypercalcemia due to malignancy. In sarcoidosis, hypercalcemia is associated with increased 1,25-(OH) 2-D_3 and serum angiotensin-converting enzyme levels; the parathyroid hormone concentration is normal. Thus, the triad of hypercalcemia, elevated serum angiotensin-converting enzyme and increased 1,25-dihydroxyvitamin D_3 strongly favor sarcoidosis as the cause of hypercalcemia.

Once the diagnosis of sarcoidosis is established, the treatment is relatively straightforward. I usually give 20 to 40 mg of prednisone daily in a single dose. For patients with severe hypercalcemia, I prefer a higher dosage—60 to 80 mg—of prednisone a day. The dose is then gradually reduced to a maintenance level of about 10 mg daily. An alternate-day regimen can be used effectively.

OM P. SHARMA, MD
Los Angeles

REFERENCES

Adams JS, Sharma OP, Gacad MA, et al: Metabolism of 25-hydroxyvitamin D_3 by cultured pulmonary alveolar macrophages in sarcoidosis. J Clin Invest 1983 Nov; 72:1856-1860

Boyd JC, Ladenson JH: Value of laboratory test in the differential diagnosis of hypercalcemia. Am J Med 1984 Nov; 77:863-872

Mason RS, Frankel T, Chan YL, et al: Vitamin D conversion by sarcoid lymph node homogenate. Ann Intern Med 1984 Jan; 100:59-61

Sharma OP: Sarcoidosis: Clinical Management. London, Butterworths, 1984, pp 145-149

Spratling L, Tenholder MF, Underwood GH, et al: Daily vs alternate day prednisone therapy for stage II sarcoidosis. Chest 1985; 88:687-690

Respiratory Muscle Fatigue

MUSCLE FATIGUE is defined as the inability to sustain a required force. The respiratory muscles behave like other skeletal muscles and fatigue develops when they are subjected to excessive loads. Muscle fatigue results from contractile failure within muscle fibers, rather than from impaired neuromuscular transmission or central nervous system fatigue. In addition to the treatment of underlying lung disease, the management of respiratory failure requires that attention be directed to the ventilatory pump itself. Factors that impair muscle contractility must be corrected. These include low cardiac output, acidosis, hypoxemia, hypercapnia and low serum levels of potassium, magnesium and phosphorus. In addition, other methods have been suggested to improve and optimize ventilatory muscle function and may be valuable both in acute conditions and for long-term benefit. These include drugs such as the methylxanthines, ventilatory muscle rest, ventilatory muscle training and nutritional supplementation.

Methylxanthines. Apart from a central stimulant effect, it is now clear that theophylline increases the contractile tension of skeletal muscle. The mechanism may be related to increased calcium release from the sarcoplasmic reticulum. Still controversial is whether the degree of enhanced contractility of the diaphragm is enough to avert respiratory failure or to provide significant clinical improvement in respiratory muscle function.

Ventilatory muscle rest. It has been suggested that chronic fatigue occurs in overloaded ventilatory muscles, leading ultimately to respiratory failure. In nonrespiratory skeletal muscle, recovery from fatigue may take several hours to days, and it has been proposed that resting the ventilatory muscle by the use of controlled mechanical ventilation may be beneficial in improving and strengthening contractility of the inspiratory muscles. Preliminary reports of nocturnal mechanical ventilation in hypercapnic patients with pulmonary and neuromuscular disease suggest that this method may be beneficial, but further control studies are necessary.

Nutrition. Undernutrition and weight loss impair ventilatory muscle strength and endurance, both of which predispose to and perpetuate respiratory failure. Nutritional repletion is important, but it must be remembered that high-calorie diets that contain a large percentage of carbohydrate produce larger quantities of carbon dioxide than do diets containing equicaloric proportions of carbohydrates and fats. Patients with impaired pulmonary function may have difficulty excreting this excess CO_2.

Ventilatory muscle training. Endurance training in general increases skeletal muscle endurance. For ventilatory muscles, there are two methods of training: one is the resistive method, in which the patient breathes at a normal rate through a high respiratory resistance, and the other is the hyperpneic method in which the patient does isocapnic hyperpnea for a prolonged period. Both these methods may improve ventilatory muscle endurance and in some studies have improved overall exercise tolerance in patients with chronic obstructive pulmonary disease. Further work is necessary to delineate the appropriate indications for training versus resting the ventilatory muscle.

The ventilatory pump is as vital to life as the heart. Understanding of the pathogenesis and reversal of ventilatory muscle fatigue is crucial to improving the management of respiratory failure.

MICHAEL J. BELMAN, MD
Duarte, California

REFERENCES

Belman MJ, Sieck GC: The ventilatory muscles: Fatigue, endurance and training. Chest 1982 Dec; 82:761-766

Moxham J, Green M: Aminophylline and the respiratory muscles. Bull Eur Physiopathol Respir 1985 Jan-Feb; 21:1-6

Roussos C, Macklem PT: The respiratory muscles. N Engl J Med 1982; 307:786-797

Continuous Monitoring of Mixed Venous Oxygen Saturation

CONTINUOUS MIXED VENOUS oxygen saturation ($S\bar{v}O_2$) monitoring is a research tool that has become commercially available for clinical use. The monitoring system consists of a light source and analyzer connected to fiber-optic bundles embedded within a pulmonary artery catheter. Oxyhemoglobin saturation is measured through the fiber-optic bundles by its predictable effect upon hemoglobin's light absorption.

$S\bar{v}O_2$ is determined by the balance between oxygen delivery and oxygen consumption. Oxygen delivery is dependent on both pulmonary and cardiovascular systems, while oxygen consumption is dependent on the clinical situation. With some exceptions, $S\bar{v}O_2$ generally functions as an indicator that overall cardiac and pulmonary function is adequate

and that tissue oxygen requirements are being met. Although $S\bar{v}O_2$ is affected by cardiac output, arterial oxygen saturation, hemoglobin and oxygen consumption, it does not consistently correlate with any of these variables in patients with critical illness such as adult respiratory distress syndrome or acute myocardial infarction.

The clinical value purported for continuous $S\bar{v}O_2$ monitoring includes an early warning of change in the oxygen delivery-consumption equilibrium, allowing prompt intervention; a continuous "on line" evaluation of the net results of pulmonary and cardiac function, allowing more rapid changes in the fraction of inspired oxygen and positive end-expiratory pressure; if the $S\bar{v}O_2$ remains stable, determination of routine arterial blood gases and hemodynamic indices may be discontinued. Pursuing fluctuations in $S\bar{v}O_2$, however, may result in frequent arterial blood gas and hemodynamic measurements of minimal clinical value. Thus, cost saving is equivocal.

The accuracy, reliability and utility of the fiber-optic catheter monitoring system have been shown. It is difficult, however, to determine whether these advantages justify the additional cost and whether they affect patient survival. Widespread clinical use of the techniques should depend on affirmative answers to both issues.

SEUNG C. YANG, MD
JAMES R. DEXTER, MD
Loma Linda, California

REFERENCES

Danek SJ, Lynch JP, Weg JG, et al: The dependence of oxygen uptake on oxygen delivery in the adult respiratory distress syndrome. Am Rev Respir Dis 1980 Sep; 122:387-395

Divertie MB, McMichan JC: Continuous monitoring of mixed venous oxygen saturation. Chest 1985 Mar; 85:423-428

Yang SC, Kyff J, Puri VK: Continuous monitoring of mixed venous oxygen saturation in patients with acute myocardial infarction (Abstr). Chest 1985 Jul; 88:66

Nasal Continuous Positive Airway Pressure—Treatment for Obstructive Sleep Apnea

THE SLEEP APNEA syndrome has a spectrum that ranges from a subclinical abnormality to a life-threatening disorder. Many therapeutic modalities exist, and physicians should choose the treatment most appropriate for an individual patient. Nasal continuous positive airway pressure (CPAP) has been used since 1981. It represents a significant advance because it is an alternative to tracheostomy in the management of severe obstructive sleep apnea.

Obstructive apnea is produced when subatmospheric intra-airway pressure, generated during inspiration, causes the tongue and soft palate to be drawn against the posterior oropharyngeal wall with resultant airway closure. The application of positive airway pressure through the nares will prevent airway closure and abolish the obstructive apnea syndrome. The mechanism by which CPAP produces this effect is still not completely defined. The simplest explanation is that the continuous positive airway pressure acts as a pneumatic splint and prevents upper airway occlusion by pushing the soft palate and tongue forward and away from the posterior oropharyngeal wall. The mechanism is likely more complex, however, and may involve stimulation of reflexes in the upper airways and the lungs.

While there has been some variation, the CPAP apparatus generally consists of four components: an air compressor or blower provides the source of high air flow; lightweight disposable respiratory tubing carries air, which may be humidified, to the patient (it is important that dynamic resistance of the tubing be kept low); a mask or other device is used to provide a tight seal about the nares; a positive end-expiratory pressure valve or a mechanical resistance, placed on the exhaust limb of the mask tubing, results in generation of positive pressure. During a nap or nighttime study, positive pressure is adjusted upward until the apneas are eliminated. The level necessary has generally ranged from 3 to 15 cm of water pressure. The major drawback to nasal CPAP is the inconvenience of nightly use of the apparatus, which some patients find cumbersome. It must be strongly emphasized that the key to the successful use of nasal CPAP is patient education and training. Skilled supervision in the initial use of the equipment and follow-up are crucial for patient compliance and success.

While nasal CPAP can be used to treat mild sleep apnea, more commonly it is used in the severe cases. Because obstructive apneas are eliminated immediately with its application, nasal CPAP is an alternative to tracheostomy in life-threatening situations. Nasal CPAP can be used until other therapeutic modalities, such as weight reduction, medications, uvulopalatopharyngoplasty or mandibular osteotomy, have effected their response. Improvement in the quality of sleep and daytime symptoms occurs rapidly after the initiation of nasal CPAP. Polysomnograms show the return of slow-wave sleep (stages III and IV) and disappearance of repeated nocturnal miniarousals. Correction of hypersomnolence enables a patient to function more productively during the day.

RICHARD A. NUSSER, MD
Oakland, California

REFERENCES

Berry RB, Block AJ: Positive nasal airway pressure eliminates snoring as well as obstructive sleep apnea. Chest 1984 Jan; 85:15-20

Kryger M (Ed): Sleep disorders. Clin Chest Med 1985 Dec; 6:553-731

Rapoport DM, Sorkin B, Garay SM, et al: Reversal of the 'Pickwickian syndrome' by long-term use of nocturnal nasal-airway pressure. N Engl J Med 1982 Oct; 307:931-933

Sullivan CE, Issa FG, Berthon-Jones M, et al: Reversal of obstructive sleep apnea by continuous positive airway pressure applied through nares. Lancet 1981 Apr; 1:862-865

Lung Abscess

WITH THE INTRODUCTION of antibiotic therapy, the incidence and mortality of lung abscess has decreased dramatically. Therapy has become primarily medical, with surgical procedures required only in rare instances. In the past decade, it became clear that anaerobic organisms are the cause of most cases of lung abscesses, particularly those that are community-acquired.

More recently, it has become apparent that the etiology of lung abscess has continued to change, with an increasing incidence of hospital-acquired (nosocomial) infections due to Gram-negative aerobic bacilli and staphylococci and opportunistic infections in immunocompromised patients. Opportunistic organisms particularly likely to cause lung abscess include atypical mycobacteria, *Nocardia, Legionella* species, *Candida* species, *Aspergillus* species and the Phycomycetes. It is critically important in such cases to determine the precise nature of the infecting organisms so that appropriate therapy